We Claim:

1. A method for attenuating expression of a target gene in cultured cells, comprising introducing double stranded RNA (dsRNA) into the cells in an amount sufficient to attenuate expression of the target gene, wherein the dsRNA comprises a nucleotide sequence that hybridizes under stringent conditions to a nucleotide sequence of the target gene.

2. A method for attenuating expression of at least one target gene in cultured cells, comprising introducing at least one double stranded RNA (dsRNA) into the cells in an amount sufficient to attenuate expression of the target gene, wherein the dsRNA comprises a nucleotide sequence that hybridizes under stringent conditions to a nucleotide sequence of the target gene.

3. A method for attenuating expression of at least one target gene in a mammalian cell, comprising introducing at least one double stranded RNA (dsRNA) into the mammalian cell in an amount sufficient to attenuate expression of the target gene, wherein the dsRNA comprises a nucleotide sequence that hybridizes under stringent conditions to a nucleotide sequence of the target gene.

4. The method of claim 1, 2 or 3, wherein the double stranded RNA (dsRNA) hybridizes under stringent conditions to coding sequence of the target gene.

5. The method of claim 1, 2, or 3, wherein the double stranded RNA (dsRNA) hybridizes under stringent conditions to non-coding sequence of the target gene.

6. The method of claim 4, wherein the non-coding sequence of the target gene is selected from the group consisting of promoter sequence, enhancer sequence, or intronic sequence.

7. A method for attenuating expression of a target gene in a mammalian cell, comprising

   (i) activating one or both of a Dicer activity or an Argonaut activity in the cell, and

   (ii) introducing into the cell a double stranded RNA (dsRNA) in an amount sufficient to attenuate expression of the target gene, wherein the dsRNA comprises a nucleotide sequence that hybridizes under stringent conditions to a nucleotide sequence of the target gene.

8. The method of claim 7, wherein the cell is suspended in culture.

9. The method of claim 7, wherein the cell is in a whole animal, such as a non-human mammal.

10. The method of any of claims 1-3 or 7, wherein the cell is engineered with (i) a recombinant gene encoding a Dicer activity, (ii) a recombinant gene encoding an Argonaut activity, or (iii) both.

11. The method of claim 10, wherein the recombinant gene encodes a protein which includes an amino acid sequence at least 50 percent identical to SEQ ID No. 2 or 4 or the Argonaut sequence shown in Figure 24.

12. The method of claim 10, wherein the recombinant gene includes a coding sequence which hybridizes under wash conditions of 2 x SSC at 22°C to SEQ ID No. 1 or 3.

13. The method of any of claims 1-3 or 7, wherein an endogenous Dicer gene or Argonaut gene is activated.

14. The method of any of claims 1-3 or 7, wherein the target gene is an endogenous gene of the cell.

15. The method of any of claims 1-3 or 7, wherein the target gene is a heterologous gene relative to the genome of the cell, such as a pathogen gene.

16. The method of any of claims 1-3 or 7, wherein the cell is treated with an agent that inhibits protein kinase RNA-activated (PKR) apoptosis, such as by treatment with agents which inhibit expression of PKR, cause its destruction, and/or inhibit the kinase activity of PKR.

17. The method of any of claims 1-3 or 7, wherein the cell is a primate cell, such as a human cell.

18. The method of any of claims 1-3 or 7, wherein the dsRNA is at least 20 nucleotides in length.

19. The method of claim 18, wherein the dsRNA is at least 100 nucleotides in length.

20. The method of any of claims 1-3 or 7, wherein expression of the target gene is attenuated by at least 10 fold.

21. An assay for identifying nucleic acid sequences responsible for conferring a particular phenotype in a cell, comprising

(i) constructing a variegated library of nucleic acid sequences from a cell in an orientation relative to a promoter to produce double stranded DNA;

(ii) introducing the variegated dsRNA library into a culture of target cells;

(iii) identifying members of the library which confer a particular phenotype on the cell, and identifying the sequence from a cell which correspond, such as being identical or homologous, to the library member.

22. A method of conducting a drug discovery business comprising:

(i) identifying, by the assay of claim 21, a target gene which provides a phenotypically desirable response when inhibited by RNAi;

(ii) identifying agents by their ability to inhibit expression of the target gene or the activity of an expression product of the target gene;

(iii) conducting therapeutic profiling of agents identified in step (b), or further analogs thereof, for efficacy and toxicity in animals; and

(iv) formulating a pharmaceutical preparation including one or more agents identified in step (iii) as having an acceptable therapeutic profile.

23. The method of claim 22, including an additional step of establishing a distribution system for distributing the pharmaceutical preparation for sale, and may optionally include establishing a sales group for marketing the pharmaceutical preparation.

24. A method of conducting a target discovery business comprising:

(i) identifying, by the assay of claim 21, a target gene which provides a phenotypically desirable response when inhibited by RNAi;

(ii) (optionally) conducting therapeutic profiling of the target gene for efficacy and toxicity in animals; and

(iii). licensing, to a third party, the rights for further drug development of inhibitors of the target gene.

25. A method for attenuating expression of a target gene in a cell, comprising introducing into the cell a hairpin nucleic acid in an amount sufficient to attenuate expression of the target gene, wherein the hairpin nucleic acid comprises an

inverted repeat of a nucleotide sequence that hybridizes under stringent conditions to a nucleotide sequence of the target gene.

26. A hairpin nucleic acid for inhibiting expression of a target gene, comprising a first nucleotide sequence that hybridizes under stringent conditions to a nucleotide sequence of the target gene, and a second nucleotide sequence which is a complementary inverted repeat of said first nucleotide sequence and hybridizes to said first nucleotide sequence to form a hairpin structure.

27. The method of claim 25 or the hairpin nucleic acid of claim 26, wherein the hairpin nucleic acid is RNA.

28. A non-human transgenic mammal having germline and/or somatic cells comprising a transgene encoding a dsRNA construct.

29. The transgenic animal of claim 28, which is chimeric for said transgene.

30. The transgenic animal of claim 28, wherein said transgene is chromosomally incorporated.

31. The transgenic animal of claim 28, wherein the dsRNA comprises a nucleotide sequence which hybridizes under stringent conditions to a nucleotide sequence of the target gene.

32. The transgenic animal of claim 31, wherein the nucleotide sequence hybridizes under stringent conditions to coding sequence of the target gene.

33. The transgenic animal of claim 31, wherein the nucleotide sequence hybridizes under stringent conditions to non-coding sequence of the target gene.

34. A double-stranded RNA for inhibiting expression of a mammalian gene, comprising a first nucleotide sequence that hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to a nucleotide sequence of at least one mammalian gene and a second nucleotide sequence which is complementary to said first nucleotide sequence.

35. The double-stranded RNA of claim 34, wherein the first nucleotide sequence of said double-stranded RNA is at least 20 nucleotides.

36. The double-stranded RNA of claim 34, wherein the first nucleotide sequence of said double-stranded RNA is at least 25 nucleotides.

37. The double-stranded RNA of claim 34, wherein the first nucleotide sequence of said double-stranded RNA is at least 100 nucleotides.

38. The double-stranded RNA of claim 34, wherein the first nucleotide sequence of said double-stranded RNA is at least 400 nucleotides.

39. The double-stranded RNA of claim 34, wherein the first nucleotide sequence of said double-stranded RNA is identical to at least one mammalian gene.

40. The double-stranded RNA of claim 34, wherein the mammalian gene is a human gene.

41. The double-stranded RNA of claim 34, wherein the double-stranded RNA is a hairpin comprising a first nucleotide sequence that hybridizes under stringent conditions to a nucleotide sequence of at least one mammalian gene, and a second nucleotide sequence which is a complementary inverted repeat of said first nucleotide sequence and hybridizes to said first nucleotide sequence to form a hairpin structure.

42. The double-stranded RNA of claim 34, wherein the double-stranded RNA is an siRNA.

43. The double-stranded RNA of claim 34, wherein the first nucleotide sequence hybridizes under stringent conditions to a nucleotide sequencing corresponding to coding sequence of at least one mammalian gene.

44. The double-stranded RNA of claim 43, wherein the first nucleotide sequence is identical to a nucleotide sequencing corresponding to coding sequence of at least one mammalian gene

45. The double-stranded RNA of claim 34, wherein the first nucleotide sequence hybridizes under stringent conditions to a nucleotide sequencing corresponding to non-coding sequence of at least one mammalian gene.

46. The double-stranded RNA of claim 45, wherein the first nucleotide sequence is identical to a nucleotide sequencing corresponding to non-coding sequence of at least one mammalian gene

47. The double-stranded RNA of claim 45, wherein the non-coding sequence is a non-transcribed sequence.